

Table 6.3 Critical Attribute Selection Using Different Threshold Calculation Formulas

Threshold Calculation Formula	CQA Risk Assessment		CPP Risk Assessment	
	Two Factors	Three Factors	Two Factors	Three Factors
$(1/5)RN_{max}$	89%	78%	99%	72%
$(1/3)RN_{max}$	89%	50%	81%	39%
$(1/2)RN_{max}$	67%	11%	53%	6%

Note: The values represent the percentage of critical attributes with respect to all attributes. Criticality can be assessed with tools using two or three factors as described above. RN_{max} represents the maximal value of the risk score (all factors at the maximum score). Values in bold represent criticality corresponding to the $T = (1/n)RN_{max}$ rule.

tool into account. Accordingly, the results suggest that $(1/n)RN_{max}$ is an appropriate formula for threshold calculation.

6.4 Iteration of risk assessment

Risk assessments deliver a rank of attributes based on the calculated RN. Moreover, attributes with a higher RN than a predefined threshold are designated as critical. Thus, the outcome of the risk assessment is the rank and the number of critical attributes. Based on these results, the most critical tasks for process development are prioritized, and the first process characterization studies are designed. The knowledge gained in these experiments can result in increased process understanding and subsequent variation in the criticality of some attributes. Therefore, the risk assessment can be revised to integrate the obtained knowledge in process development decisions (see Figure 6.7).

The use of inappropriate factors in the risk assessment tool can lead to an unexpected rank of the attributes. In such cases, the risk assessment tool itself has to be revised and the factors modified.

Although the outcome of risk assessments can be modified by iterative processes shown in Figure 6.7, the predefined goal has to be considered to avoid missing the aim of the risk assessment. In other words, the revisions and subsequent adjustments in the threshold value or the risk assessment tool should not compromise patient safety for the simplification of product development.

Another interesting issue in risk management is the handling of non-critical data. Variables with a lower score than the risk threshold are designated as noncritical and do not have to be included further in the description of design space. However, the assessment of criticality is not static and it might change with the increase of product and process understanding. Consequently, noncritical variables can become critical